SUPPLEMENTAL MATERIAL

Consumption of fluoridated water is believed to offer protection against the development of dental caries in children (McDonagh et al. 2000). Although water supplies are not uniformly fluoridated throughout the U.S. – neither now nor at the time of this survey – data on water fluoridation pertaining to the NHANES III participants were not readily available at the time of this report. We conducted a sensitivity analysis to evaluate potential confounding by water fluoridation using software developed by Schneeweiss (2006). In this analysis, we assumed that 46% of the children in our study consumed non-fluoridated water (CDC 2006) (i.e., $P_{NFW} = 0.46$) and that consumption of non-fluoridated water increased the risk of developing any caries by a minimum of 15% (McDonagh et al. 2000) up to 50%, the latter estimate representing a more extreme hypothetical association (i.e., $RR_{NFW\text{-}Caries} = 1.15$ to 1.50). We then evaluated potential confounding by consumption of fluoridated water, over the range of $RR_{NWF\text{-}Caries}$ and over a range of associations between fluoridated water consumption and creatinine-corrected urinary cadmium (i.e., $OR_{NFW\text{-}Cd}$).

The approach to this sensitivity analysis requires an estimate of the apparent relative risk (or prevalence) ratio (ARR) relating the exposure (cadmium exposure) to the outcome (any caries). We derived such an estimate of the ARR from our multivariable-adjusted logistic regression model, standardizing it to the age structure of our study population (Greenland 2004). For simplicity, we dichotomized creatinine-corrected urinary cadmium levels in our study population at the median. After adjusting for the covariates that were in our full model, children with cadmium levels above the median had a 60% increase in the odds of developing carious surfaces – equivalently, the

apparent risk ratio, ARR = 1.19. With this and the previously described parameters (prevalence of non-fluoridated water consumption, $P_{NFW} = 0.46$; association between non-fluoridated water consumption, $RR_{NFW\text{-}Caries} = 1.15$ to 1.50), we determined that with $RR_{NFW\text{-}Caries} = 1.15$, no magnitude of association between non-fluoridated water consumption and urinary cadmium ($OR_{NFW\text{-}Cd}$) would fully account for the observed association between cadmium and caries. Even with an extreme $OR_{NFW\text{-}Cd}$ in which the prevalence of non-fluoridated water consumption was 70% among children in the high-cadmium group and 22% among children in the low-cadmium group ($OR_{NFW\text{-}Cd} = 8.3$), the cadmium-caries RR would have been 1.11 after adjusting for water fluoridation, instead of 1.19. As expected, when we assumed that $RR_{NFW\text{-}Caries} = 1.50$, a less exceptional disparity in cadmium level by water fluoridation status could influence the observed cadmium-caries association. For example, assuming that 51% and 41% of high-cadmium and low-cadmium children consumed non-fluoridated water ($OR_{NFW\text{-}Cd} = 2.1$), the adjusted cadmium-caries RR would have been 1.14 instead of 1.19. Even so, with $RR_{NFW\text{-}Caries} = 1.50$, non-fluoridated water consumption could *fully* account for our findings only if $OR_{NFW\text{-}Cd} = 6.1$ (i.e., if the prevalence of non-fluoridated water consumption was 67% and 25% in the high and low cadmium groups). Based on these results, it appears unlikely that differences in water fluoridation by cadmium exposure (at least in the direct manner we have described) could explain a substantial portion of the observed association between cadmium exposure and caries experience.

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